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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
FPW/P92708WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/00913	13/03/2000	13/03/1999
International Patent Classification (IPC) or national classification and IPC A61L27/00		
Applicant BIOINTERACTIONS LTD. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 5 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
09/10/2000	28.05.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Peris Antoli, B Telephone No. +49 89 2399 8476

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/00913

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-15	as originally filed				

Claims, No.:

1-35	as received on	07/05/2001	with letter of	03/05/2001	

Drawings, sheets:

1/8-8/8	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)
   see separate sheet

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1,2,4,6-35
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1,2,4,6-35
Industrial applicability (IA)	Yes:	Claims	1,2,4,6-35
	No:	Claims	

2. Citations and explanations
   see separate sheet

Re Item I

Basis of the report

1. The amendments filed with the letter dated 03.05.01 introduce subject-matter which extends beyond the content of the application as filed, contrary to Article 34(2)(b) PCT. The amendments concerned are the following:

   (i) The restriction in the new claim 3 to copolymerization of **only two** monomers of the classes specified in previous claims. [Said particular restriction was not disclosed in the application as originally filed].

   (ii) The introduction in claim 5 of a **tubular** flexible **material** being an **hydrogel**. [Note that p. 15, l. 1-2 of the original application only discloses that the biocompatible coating or encapsulating the endoprosthesis can be in the form of an hydrogel]

2. According to R. 70.2(c) PCT this report has been established as if the aforementioned claims 3 and 5 has not been filed.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

3. Reference is made to the following documents:

   D1 = EP-A-0 797 963
   D2 = DE-A-195 24 653
   D3 = WO-A-97 41164
   D4 = DE-A-44 07 079

4. The subject matter of independent claim 1 and that of its dependent claims 2, 4, 6-35 is new over the prior art cited in the search report, because none of the cited documents discloses a endoprosthesis comprising an array of consecutive aligned cylindrical stent elements in conjunction with a one-piece tubular flexible material (i.e. and stent covered by a continuous tubular element), said endoprosthesis

being totally coated with or encapsulated in a polymer obtainable by copolymerization of monomers as specified in items a) to e) of claim 1.

4.1 Thus, claims 1-33 meet the requirements of Art. 33(2) PCT.

5. Claims 1, 2, 4, 6-33 do however not meet the requirements of Art. 33(3) PCT for the reasons set out below.

5.1 As acknowledged in the application (see e.g. p. 3, l. 10-17 and passage bridging pp. 3-4), endoprosthesis comprising an stent covered by a continuous (porous) tubular element are already known from the state of the art. With this respect see e.g. D1 (claims 1, 5, 6 and Fig. 8) and D2 (claims 5-7 und Figs 2 and 4). Endoprosthesis having an array of consecutive aligned cylindrical stent elements constructed of wire wound in zigzag form are also known from the state of the art; see e.g. D4: c. 2, l. 12-15, 59-62; c. 3, l. 46-51 and Figs. 1, 7 and 10. As also acknowledged in the application, it is known that the continuous tubular element is designed to form a barrier to prevent tissue re-growth. As stated In the application, the materials used for both the stent and the covering tubular element are however thrombogenic to some degree, so that tissue re-growth and the possibility of re-stenosis is not highly prevented.

5.2 The problem posed in the present application was to provide stent devices to treat stenosis, which also reduce or prevent restenosis after interventional treatment.

5.3 As proposed in the claims, said problem is solved with an endoprosthesis comprising a stent constructed of wire wound in zigzag form and which is covered by a continuous tubular flexible material, wherein said endoprosthesis is totally coated with or encapsulated in a polymer obtained by copolymerization of monomers as specified in claim 1.

5.4 As acknowledged in the application (see e.g. p. 5. l. 28-34), the polymeric material specified in the present claim 1 is already known from D3 (see e.g. claim 1). Said material is known to be biocompatible, non-thrombogenic and suitable to modification by the introduction of anti-thrombogenic compounds, so as to provide a material that is both non-thrombogenic and anti-thrombogenic (see D3: passage

bridging pp. 3-4). As indicated in D3 (see p. 3, paragraphs 2 and 3) such a non-thrombogenic and anti-thrombogenic polymeric material will prevent both clot formation and deposition of proteins, platelets and blood cells thereon. As also indicated in D3 (see e.g. p. 14, third paragraph, claim 14 and example 15), said polymeric material can be used for coating medical devices for use in blood-contacting applications, such as tubings.

5.5 Since the aforementioned properties of non-thrombogenic and anti-thrombogenic polymeric are the ones required to prevent tissue re-growth, those skilled in the art aware of the teachings of D3, would have found it obvious to coat known endoprosthesis (as is the case of those disclosed in D4 which have the same stent configuration as that specified in the present claim 1) to reduce or prevent restenosis and hence to solve the problem posed.

5.6 Thus, no inventive step can be recognised for the subject matter of the present 1,2, 4, 6-35 claims.

6. Claims 1, 2, 4, 6-35 satisfy the criterion set forth in Art. 33(4) PCT because their subject matter is susceptible of industrial application.

CLAIMS

1. A flexible endoprosthesis comprising an array of consecutive aligned cylindrical stent elements in the form of a plurality of sequentially connected radially stable outwardly biased cylindrical springs constructed of wire wound in zigzag form and a one-piece tubular flexible material maintained in open tubular form by the array of stent elements, the array of stent elements and the tubular flexible material together being totally coated with or encapsulated in a polymer comprising a polymer backbone having pendant groups, obtainable by polymerizing monomers having such groups, characterized in that said polymers are obtained by copolymerizing monomers of at least two different classes selected from:

a) monomers having sulphate groups
b) monomers having sulphonate groups
c) monomers having sulphamate groups
d) monomers having polyoxyalkylene ether groups, and
e) monomers having zwitterionic groups

2. An endoprosthesis as claimed in claim 1, characterized in that said polymers are obtained by copolymerizing monomers of at least two different classes selected from:

a) monomers having sulphate groups
b) monomers having sulphonate groups
c) monomers having sulphamate groups, and
d) monomers having polyoxyalkylene ether groups

3. An endoprosthesis as claimed in claim 1 or 2 characterized in that the polymers are obtained by copolymerizing monomers of two only of the respective said different classes.

4. An endoprosthesis as claimed in any one of claims 1 to 3 characterized in that the polymer comprises an additional comonomer having pendant heparin, hirudin, warfarin or hyaluronic acid groups.

5. An endoprosthesis as claimed in any one of claims 1 to 4 characterized in that the polymer encapsulates the array of stent elements and the tubular flexible material as a hydrogel.

6. An endoprosthesis as claimed in any one of claims 1 to 5 characterized in that the stent elements are permanently attached to the array of cylindrical stent elements.

7. An endoprosthesis as claimed in claim 6 characterized in that the tubular flexible material is attached by sewing, welding, an adhesive or mechanical clips.

8. An endoprosthesis as claimed in any one of claims 1 to 7 characterized in that the tubular flexible material is inside the stent elements.

9. An endoprosthesis as claimed in any one of claims 1 to 7 characterized in that the tubular flexible material is outside the stent elements.

10. An endoprosthesis as claimed in any one of claims 1 to 7 characterized in that the stent elements are sandwiched between two flexible tubes.

11. An endoprosthesis as claimed in any one of claims 1 to 7 characterized in that the stent elements are encapsulated by the tubular flexible material.

12. An endoprosthesis as claimed in any of claims 1 to 10 characterized in that the tubular flexible material is a textile fabric, a woven fabric, or a knitted fabric.

13. An endoprosthesis as claimed in claim 12 characterized in that the woven or knitted fabric is made from a polyester yarn.

14. An endoprosthesis as claimed in any of claims 1 to 12 characterized in that the tubular flexible material is a continuous tubular element or film.

15. An endoprosthesis as claimed in claim 14 characterized in that the continuous tubular element or film is formed from a synthetic polymer.

16. An endoprosthesis as claimed in claim 15 characterized in that the synthetic polymer is a polyester, or a polyurethane.

17. An endoprosthesis as claimed in claim 14 characterized in that the continuous tubular element or film is formed from an elastomer.

18. An endoprosthesis as claimed in claim 17 characterized in that the elastomer is silicone rubber or polytetrafluoroethylene.

19. An endoprosthesis as claimed in any of claims 1 to 18 characterized in that the stent elements are composed of a wire, wound, in zigzag form into a cylindrical shape.

20. An endoprosthesis as claimed in claim 19 characterized in that the wire has a circular cross section or is a flat tape.

21. An endoprosthesis as claimed in any of claims 1 to 18 characterized in that the stent elements are constructed from a metallic or polymeric tube by laser cutting or chemical etching.

22. An endoprosthesis as claimed in claim 21 characterized in that the wire of each stent element has both ends connected to each other so as to have a continuous form.

23. An endoprosthesis as claimed in claim 19 characterized in that the ends of the wire of each stent element are joined by overlapping and binding with suture material.

24. An endoprosthesis as claimed in any of claims 1 to 19 characterized in that the individual stent elements are made from a continuous length of wire so that they remain connected to each other.

25. An endoprosthesis as claimed in any of claims 17 to 24 characterized in that the stent elements are made from spring-tempered metal.

26. An endoprosthesis as claimed in claim 25 characterized in that the spring-tempered metal is stainless steel.

27. An endoprosthesis as claimed in any of claims 17 to 24 characterized in that the stent elements are made from a shape memory alloy.

28. An endoprosthesis as claimed in claim 27 characterized in that the shape memory alloy wire is martensitic at temperatures lower than 37°C.

29. An endoprosthesis as claimed in claim 27 characterized in that the shape memory alloy wire is austenitic at or above a temperature of 37°C.

30. An endoprosthesis as claimed in claim 27 characterized in that the shape memory alloy wire is in superelastic form at or above a temperature of 37°C.

31. An endoprosthesis as claimed in any of claims 17 to 24 characterized in that the stent elements are made from a malleable material.

32. An endoprosthesis as claimed in claim 31 characterized in that the malleable material is malleable stainless steel.

33. An endoprosthesis as claimed in any of claims 1 to 32 characterized in that the individual stent elements are arranged so as not to touch each other or to interfere with each other so as to give maximum flexibility to the complete device during delivery and subsequent operation.

34. An endoprosthesis as claimed in any of claims 1 to 32 characterized in that the individual stent elements are arranged so as to be alternately of opposite phase with the apexes of the zigs in one stent element in contact with the next, so as to give maximum stability to the device during delivery.

35. An endoprosthesis as claimed in claim 1 to 32 characterized in that the connections between individual stent elements are bound together to form a longitudinal spine in the complete device.